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## RAW SEQUENCE LISTING

PATENT APPLICATION: PCT/US02/21090

DATE: 07/24/2002

TIME: 11:49:19

Input Set : A:\Sequence

Output Set: N:\CRF3\07242002\PU21090.raw

#11/K.T.  
8/20  
Raw  
Seq.  
Listing

```

3 <110> APPLICANT: Isis Pharmaceuticals, Inc.
4   C. Frank Bennett
5   Susan M. Freier
7 <120> TITLE OF INVENTION: ANTISENSE MODULATION OF HKR1 EXPRESSION
9 <130> FILE REFERENCE: RTSP-0386
C--> 11 <140> CURRENT APPLICATION NUMBER: PCT/US02/21090
C--> 11 <141> CURRENT FILING DATE: 2002-07-02
11 <150> PRIOR APPLICATION NUMBER: 09/898,556
12 <151> PRIOR FILING DATE: 2001-07-03
14 <160> NUMBER OF SEQ ID NOS: 89
17 <210> SEQ ID NO: 1
18 <211> LENGTH: 20
19 <212> TYPE: DNA
20 <213> ORGANISM: Artificial Sequence
22 <220> FEATURE:
24 <223> OTHER INFORMATION: Antisense Oligonucleotide
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30 <210> SEQ ID NO: 2
31 <211> LENGTH: 20
32 <212> TYPE: DNA
33 <213> ORGANISM: Artificial Sequence
35 <220> FEATURE:
37 <223> OTHER INFORMATION: Antisense Oligonucleotide
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40   atgcattctg cccccaagga                                20
43 <210> SEQ ID NO: 3
44 <211> LENGTH: 2772
45 <212> TYPE: DNA
46 <213> ORGANISM: Homo sapiens
48 <220> FEATURE:
50 <221> NAME/KEY: CDS
51 <222> LOCATION: (3)...(2096)
53 <400> SEQUENCE: 3
54   ca ggc gcg tta agc tgg ttg gga ccc ggg aag gcc tcc ctc tta agg      47
55   Gly Ala Leu Ser Trp Leu Gly Pro Gly Lys Ala Ser Leu Leu Arg
56   1           5           10           15
58   tct ttc cca cac ctc tgc tcc ttg tta cct gac ttt cgg ctt cag gat      95
59   Ser Phe Pro His Leu Cys Ser Leu Leu Pro Asp Phe Arg Leu Gln Asp
60           20           25           30
62   ccg cgg cgt gca ccc gcg ttc cat ctg tct tct gag act ttg ccc ttc      143
63   Pro Arg Arg Ala Pro Ala Phe His Leu Ser Ser Glu Thr Leu Pro Phe
64           35           40           45

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66	tcc agg aag agc act cag gag acc agg aaa atg gct aca ggg ctc ctg	191
67	Ser Arg Lys Ser Thr Gln Glu Thr Arg Lys Met Ala Thr Gly Leu Leu	
68	50 55 60	
70	aga gcc aaa aaa gag gcg ttc gtg gca ttc agg gat gtg gct gtg tac	239
71	Arg Ala Lys Lys Glu Ala Phe Val Ala Phe Arg Asp Val Ala Val Tyr	
72	65 70 75	
74	ttc acc cag gag gag tgg agg ttg ttg agc cct gct cag agg acc ctg	287
75	Phe Thr Gln Glu Glu Trp Arg Leu Leu Ser Pro Ala Gln Arg Thr Leu	
76	80 85 90 95	
78	cac agg gag gtg atg ctg gag act tat aac cat ctg gtc tca ctg gaa	335
79	His Arg Glu Val Met Leu Glu Thr Tyr Asn His Leu Val Ser Leu Glu	
80	100 105 110	
82	att cca tct tct aaa cca aaa ctc att gct cag ctg gag cga ggg gaa	383
83	Ile Pro Ser Ser Lys Pro Lys Leu Ile Ala Gln Leu Glu Arg Gly Glu	
84	115 120 125	
86	gcg ccc tgg aga gag gag aga aaa tgt cca ctg gac ctc tgt cca gaa	431
87	Ala Pro Trp Arg Glu Glu Arg Lys Cys Pro Leu Asp Leu Cys Pro Glu	
89	130 135 140	
91	tcg aag cca gaa att caa ctt agt ccc tcc tgc cct ctg att ttc tcc	479
92	Ser Lys Pro Glu Ile Gln Leu Ser Pro Ser Cys Pro Leu Ile Phe Ser	
93	145 150 155	
95	agt cag caa gct ctc agc caa cat gtg tgg ctg agt cat ctc tct cag	527
96	Ser Gln Gln Ala Leu Ser Gln His Val Trp Leu Ser His Leu Ser Gln	
97	160 165 170 175	
99	ctg ttt tca agt tta tgg gca gga aat cct ctc cac ctg gga aaa cac	575
100	Leu Phe Ser Ser Leu Trp Ala Gly Asn Pro Leu His Leu Gly Lys His	
101	180 185 190	
103	tat cca gaa gat cag aaa caa cag cag gat cca ttc tgc ttt agt ggc	623
104	Tyr Pro Glu Asp Gln Lys Gln Gln Gln Asp Pro Phe Cys Phe Ser Gly	
105	195 200 205	
107	aaa gca gaa tgg att caa gag gga gaa gac tcc aga ctc ctg ttt ggg	671
108	Lys Ala Glu Trp Ile Gln Glu Gly Glu Asp Ser Arg Leu Leu Phe Gly	
109	210 215 220	
111	aga gta agc aaa aat ggc act tca aag gca ctt tcc agc cca cct gaa	719
112	Arg Val Ser Lys Asn Gly Thr Ser Lys Ala Leu Ser Ser Pro Pro Glu	
113	225 230 235	
115	gaa caa cag cca gca cag tcc aag gaa gac aac aca gtg gtg gat ata	767
116	Glu Gln Gln Pro Ala Gln Ser Lys Glu Asp Asn Thr Val Val Asp Ile	
117	240 245 250 255	
119	ggg tcc agc cct gaa cgg agg gca gat cta gag gaa aca gac aaa gta	815
120	Gly Ser Ser Pro Glu Arg Arg Ala Asp Leu Glu Glu Thr Asp Lys Val	
121	260 265 270	
123	ttg cat ggt tta gaa gtc tca gga ttt gga gaa atc aaa tat gaa gag	863
124	Leu His Gly Leu Glu Val Ser Gly Phe Gly Glu Ile Lys Tyr Glu Glu	
125	275 280 285	
127	ttt ggg cca ggc ttt atc aag gag tca aac ctc ctt agc ctc cag aag	911
128	Phe Gly Pro Gly Phe Ile Lys Glu Ser Asn Leu Leu Ser Leu Gln Lys	
129	290 295 300	
131	aca caa act ggg gag aca cct tac atg tac act gag tgg gga gac agc	959

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132	Thr	Gln	Thr	Gly	Glu	Thr	Pro	Tyr	Met	Tyr	Thr	Glu	Trp	Gly	Asp	Ser	
133		305					310					315					
135	ttt	ggc	agt	atg	tca	gtc	ctc	atc	aaa	aac	cca	agg	aca	cac	tct	ggg	1007
136	Phe	Gly	Ser	Met	Ser	Val	Leu	Ile	Lys	Asn	Pro	Arg	Thr	His	Ser	Gly	
137		320					325					330				335	
139	gga	aag	cct	tat	gtg	tgc	agg	gaa	tgt	ggg	cga	ggc	ttt	acg	tgg	aag	1055
140	Gly	Lys	Pro	Tyr	Val	Cys	Arg	Glu	Cys	Gly	Arg	Gly	Phe	Thr	Trp	Lys	
141						340					345					350	
143	tca	aac	ctg	atc	aca	cat	cag	agg	aca	cac	tca	ggg	gag	aaa	cct	tat	1103
144	Ser	Asn	Leu	Ile	Thr	His	Gln	Arg	Thr	His	Ser	Gly	Glu	Lys	Pro	Tyr	
145						355					360					365	
147	gtg	tgc	aag	gat	tgt	gga	cga	ggc	ttt	act	tgg	aag	tcg	aac	ctc	ttt	1151
148	Val	Cys	Lys	Asp	Cys	Gly	Arg	Gly	Phe	Thr	Trp	Lys	Ser	Asn	Leu	Phe	
149			370					375					380				
151	aca	cat	cag	cgg	aca	cac	tca	ggg	ctc	aag	cct	tat	gtg	tgc	aag	gaa	1199
152	Thr	His	Gln	Arg	Thr	His	Ser	Gly	Leu	Lys	Pro	Tyr	Val	Cys	Lys	Glu	
153		385					390					395					
155	tgt	ggg	cag	agc	ttt	agc	ctg	aag	tca	aac	ctc	att	acc	cac	cag	agg	1247
156	Cys	Gly	Gln	Ser	Phe	Ser	Leu	Lys	Ser	Asn	Leu	Ile	Thr	His	Gln	Arg	
157		400				405					410					415	
159	gcg	cac	act	ggg	gag	aag	cct	tat	gtt	tgc	agg	gaa	tgt	ggg	cgt	ggc	1295
160	Ala	His	Thr	Gly	Glu	Lys	Pro	Tyr	Val	Cys	Arg	Glu	Cys	Gly	Arg	Gly	
161					420						425					430	
163	ttt	cgc	cag	cat	tca	cac	ctg	gtc	aga	cac	aag	agg	aca	cat	tca	gga	1343
164	Phe	Arg	Gln	His	Ser	His	Leu	Val	Arg	His	Lys	Arg	Thr	His	Ser	Gly	
165			435						440					445			
167	gag	aag	cct	tac	att	tgc	agg	gag	tgt	gag	caa	ggc	ttt	agc	cag	aag	1391
168	Glu	Lys	Pro	Tyr	Ile	Cys	Arg	Glu	Cys	Glu	Gln	Gly	Phe	Ser	Gln	Lys	
169			450					455				460					
171	tca	cac	ctc	atc	aga	cac	tta	agg	aca	cac	aca	gga	gag	aag	cct	tat	1439
172	Ser	His	Leu	Ile	Arg	His	Leu	Arg	Thr	His	Thr	Gly	Glu	Lys	Pro	Tyr	
173		465					470					475					
175	gta	tgc	aca	gaa	tgt	ggg	cgt	cac	ttt	agc	tgg	aaa	tca	aac	ctc	aaa	1487
176	Val	Cys	Thr	Glu	Cys	Gly	Arg	His	Phe	Ser	Trp	Lys	Ser	Asn	Leu	Lys	
177		480				485					490					495	
179	aca	cac	cag	agg	aca	cac	tca	ggg	gtt	aaa	cct	tat	gtc	tgc	ctg	gag	1535
180	Thr	His	Gln	Arg	Thr	His	Ser	Gly	Val	Lys	Pro	Tyr	Val	Cys	Leu	Glu	
181					500					505					510		
183	tgc	ggg	cag	tgc	ttt	agc	ctg	aag	tca	aac	ctt	aac	aaa	cac	cag	agg	1583
184	Cys	Gly	Gln	Cys	Phe	Ser	Leu	Lys	Ser	Asn	Leu	Asn	Lys	His	Gln	Arg	
185			515						520				525				
187	tca	cac	acg	ggg	gag	aag	cca	ttt	gta	tgt	acg	gag	tgt	ggg	cga	ggc	1631
188	Ser	His	Thr	Gly	Glu	Lys	Pro	Phe	Val	Cys	Thr	Glu	Cys	Gly	Arg	Gly	
189			530					535					540				
191	ttt	acc	cgg	aaa	tca	acc	ctg	atc	acg	cac	cag	agg	aca	cac	tca	ggg	1679
192	Phe	Thr	Arg	Lys	Ser	Thr	Leu	Ile	Thr	His	Gln	Arg	Thr	His	Ser	Gly	
193		545					550					555					
195	gag	aag	cca	ttt	gta	tgt	gct	gag	tgt	gga	cga	ggc	ttt	aat	gat	aag	1727
196	Glu	Lys	Pro	Phe	Val	Cys	Ala	Glu	Cys	Gly	Arg	Gly	Phe	Asn	Asp	Lys	

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197      560                      565                      570                      575
199      tcc acc ctc att tca cac cag agg aca cat tca ggg gaa aag cct ttt      1775
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201      580                      585                      590
203      atg tgc agg gag tgt ggc aga agg ttt cgg cag aag cct aac ctg ttt      1823
204      Met Cys Arg Glu Cys Gly Arg Arg Phe Arg Gln Lys Pro Asn Leu Phe
205      595                      600                      605
207      agg cac aag agg gca cac tca ggt gcc ttt gtg tgc agg gag tgt ggg      1871
208      Arg His Lys Arg Ala His Ser Gly Ala Phe Val Cys Arg Glu Cys Gly
209      610                      615                      620
211      caa ggc ttt tgt gct aag tta act ctc att aaa cac cag aga gca cac      1919
212      Gln Gly Phe Cys Ala Lys Leu Thr Leu Ile Lys His Gln Arg Ala His
213      625                      630                      635
215      gca ggg ggg aag cct cat gtg tgc agg gag tgt ggg caa ggc ttt agc      1967
216      Ala Gly Gly Lys Pro His Val Cys Arg Glu Cys Gly Gln Gly Phe Ser
217      640                      645                      650                      655
219      cgg cag tca cac ctc att aga cac cag agg aca cat tca gga gag aag      2015
220      Arg Gln Ser His Leu Ile Arg His Gln Arg Thr His Ser Gly Glu Lys
221      660                      665                      670
223      cct tat att tgc aga aag tgt gga cgg ggc ttt agt cgg aag tcc aac      2063
224      Pro Tyr Ile Cys Arg Lys Cys Gly Arg Gly Phe Ser Arg Lys Ser Asn
225      675                      680                      685
227      ctt atc aga cat cag agg aca cac tca gga tag aaactttatg tgtataggga      2116
228      Leu Ile Arg His Gln Arg Thr His Ser Gly
W--> 229      675                      680
231      atgtggtaca gccttagcc aggagtcata cttcatcaga caccagagga cacacacagt      2176
232      gctgtggctt ttccagccat tgctagatac caaagtggag acattctgtg tgtgattatg      2236
233      catgagactg tactggttaag acttgtatct ccatccacct gaaggagaat tgctggctca      2296
234      ttttcaggag ccttgccctt cctcactgtg gatggtgggt tgtggaaacc cggtcaggta      2356
235      atgatagtgg caggaggcag tcaaattgcc aggcagatag ggggtgggtac ctggtgaaac      2416
236      ccaaccttaa agctgaagac agtcccggct aaatcctcat actgaattga gaacctgtct      2476
237      tcccatttgg tgtgttttcc tccgattgat cccaaccctt cacctatttt acgtatacct      2536
238      gccctttcct aattggtttt tacactgctg tgcccacctt ttgagtgggt cctttgcata      2596
239      cttacaaatc agtcaacgtg tattccccta ttctgagccc ataaaagacc cagactcagc      2656
240      tgcaagtagg agagaaatca ccctgctgtg gaggttgggg accactccct gcatcccctc      2716
241      tccactgaga gctgttcttt tgctcaataa aattcttttc taccatcct caccct      2772
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247 <213> ORGANISM: Artificial Sequence
249 <220> FEATURE:
250 <223> OTHER INFORMATION: PCR Primer
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257 <211> LENGTH: 19
258 <212> TYPE: DNA
259 <213> ORGANISM: Artificial Sequence
261 <220> FEATURE:

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262 <223> OTHER INFORMATION: PCR Primer
264 <400> SEQUENCE: 5
265     acctgaccgg gtttccaca                                19
268 <210> SEQ ID NO: 6
269 <211> LENGTH: 25
270 <212> TYPE: DNA
271 <213> ORGANISM: Artificial Sequence
273 <220> FEATURE:
274 <223> OTHER INFORMATION: PCR Probe
276 <400> SEQUENCE: 6
277     ctgcccttcc tcactgtgga tgggtg                                25
280 <210> SEQ ID NO: 7
281 <211> LENGTH: 19
282 <212> TYPE: DNA
283 <213> ORGANISM: Artificial Sequence
285 <220> FEATURE:
286 <223> OTHER INFORMATION: PCR Primer
288 <400> SEQUENCE: 7
289     gaaggtgaag gtcggagtc                                19
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293 <211> LENGTH: 20
294 <212> TYPE: DNA
295 <213> ORGANISM: Artificial Sequence
297 <220> FEATURE:
298 <223> OTHER INFORMATION: PCR Primer
300 <400> SEQUENCE: 8
301     gaagatgggtg atgggatttc                                20
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305 <211> LENGTH: 20
306 <212> TYPE: DNA
307 <213> ORGANISM: Artificial Sequence
309 <220> FEATURE:
310 <223> OTHER INFORMATION: PCR Probe
312 <400> SEQUENCE: 9
313     caagcttccc gttctcagcc                                20
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317 <211> LENGTH: 11173
318 <212> TYPE: DNA
319 <213> ORGANISM: Homo sapiens
321 <400> SEQUENCE: 10
322     aagcttcttg gctctctaag ttttattttc tattcactgt gagaagtact tggctattat    60
324     ttcaatatatt ttcctgtccc ttttactctt tcctctcatt ctaggactcc caatttacct    120
326     gtatatggga ctgctggaaa tgtgtttctg aagattcata ttgtctcata agcttctgtt    180
328     catttttctt cagtcttttt tctctttttt gaggggtggg tggatatatg taatttctat    240
330     tcttttattt tcaaattcac taatctttct tctttttctg tttgctatta aacctgtcta    300
332     gtgaattttt aaatttcagt tgtttttttc tttccccctc ccctcctctc ccctcctctc    360
334     ccctccccct ccctccccct ccctccccct ccctccccct ccctccccct ctcttgtttc    420
336     tgtgggtttt aggagtgtct tcaggcaaga aagccacaaa caaaattatt acccctttct    480
338     gttgcaattt tttgagcata aactcttccc catcttctgg ctggttatgt atattttcca    540

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RAW SEQUENCE LISTING ERROR SUMMARY  
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Invalid Line Length:

The rules require that a line not exceed 72 characters in length. This includes spaces.

Seq#:3; Line(s) 83,87,92

**VERIFICATION SUMMARY**

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L:11 M:270 C: Current Application Number differs, Replaced Current Application No  
L:11 M:271 C: Current Filing Date differs, Replaced Current Filing Date  
L:229 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3